

regard as adulterated any interstate shipment of the food seeds wheat, corn, oats, rye, barley, and sorghum bearing a poisonous treatment in excess of a recognized tolerance or treatment for which no tolerance or exemption from tolerance is recognized in regulations promulgated pursuant to section 408 of the Federal Food, Drug, and Cosmetic Act, unless such seeds have been adequately denatured by a suitable color to prevent their subsequent inadvertent use as food for man or feed for animals.

(c) Attention is called to the labeling requirements of the Federal Hazardous Substances Act, where applicable to denatured seeds in packages suitable for household use.

§ 2.35 Use of secondhand containers for the shipment or storage of food and animal feed.

(a) Investigations by the Food and Drug Administration, the National Communicable Disease Center of the U.S. Public Health Service, the Consumer and Marketing Service of the U.S. Department of Agriculture, and by various State public health agencies have revealed practices whereby food and animal feed stored or shipped in secondhand containers have been rendered dangerous to health. Such contamination has been the result of the original use of these containers for the storage and shipment of articles containing or bearing disease organisms or poisonous or deleterious substances.

(b) The Commissioner concludes that such dangerous or potentially dangerous practices include, but are not limited to, the following:

(1) Some vegetable growers and packers employ used poultry crates for shipment of fresh vegetables, including cabbage and celery. Salmonella organisms are commonly present on dressed poultry and in excreta and fluid exudates from dressed birds. Thus wooden crates in which dressed poultry has been iced and packed are potential sources of Salmonella or other enteropathogenic microorganisms that may contaminate fresh vegetables which are frequently consumed without heat treatment.

(2) Some potato growers and producers of animal feeds use secondhand

bags for shipment of these articles. Such bags may have originally been used for shipping or storing pesticide-treated seed or other articles bearing or containing poisonous substances. Thus these secondhand bags are potential sources of contamination of the food or animal feed stored or shipped therein.

(c) In a policy statement issued April 11, 1968, the Food and Drug Administration declared adulterated within the meaning of section 402(a) of the Federal Food, Drug, and Cosmetic Act shipments of vegetables or other edible food in used crates or containers that may render the contents injurious to health. This policy statement is extended so that the Food and Drug Administration will regard as adulterated within the meaning of section 402(a) of the act shipments of vegetables, other edible food, or animal feed in used crates, bags, or other containers that may render the contents injurious to health.

Subparts C-E [Reserved]

Subpart F—Caustic Poisons

§ 2.110 Definition of ammonia under Federal Caustic Poison Act.

For the purpose of determining whether an article containing ammonia is subject to the Federal Caustic Poison Act, the ammonia content is to be calculated as NH_3 .

Subpart G—Provisions Applicable to Specific Products Subject to the Federal Food, Drug, and Cosmetic Act

§ 2.125 Use of chlorofluorocarbon propellants in self-pressurized containers.

(a) As used in this section:

(1) *Chlorofluorocarbon* means any fully halogenated chlorofluoroalkane.

(2) *Propellant* means a liquefied or compressed gas that is used in whole or in part to expel from the same self-pressurized container or from a separate container a liquid or solid material different from the propellant, but the term does not include the use of a chlorofluorocarbon as an aerating

agent for foamed or sprayed food products.

(b) Chlorofluorocarbons are widely used in products subject to the Federal Food, Drug, and Cosmetic Act, with the principal use being as propellants in self-pressurized containers. Information recently developed indicates that chlorofluorocarbons may reduce the amount of ozone in the stratosphere and thus increase the amount of ultraviolet radiation reaching the earth. An increase in ultraviolet radiation may increase the incidence of skin cancer, change the climate, and produce other effects of unknown magnitude on humans, animals, and plants. Chlorofluorocarbons may also affect the climate by increasing infrared absorption in the atmosphere.

(c) Except as provided in paragraph (e) of this section, any food, drug, device, or cosmetic in a self-pressurized container that contains a chlorofluorocarbon propellant is adulterated and/or misbranded in violation of the act, and any drug product in a self-pressurized container that contains a chlorofluorocarbon propellant is a new drug or a new animal drug.

(d) The use of a chlorofluorocarbon as a propellant in a self-pressurized container of a drug product will not result in the drug product being adulterated and/or misbranded provided a new drug application, a new animal drug application, or in the case of a certifiable antibiotic an antibiotic application for the drug product has been approved, a petition has been filed as provided by paragraph (f) of this section, and paragraph (e) of this section has been amended to specify the use as essential.

(e) The adulteration and misbranding provisions of paragraph (c) of this section shall not apply to the following essential uses of chlorofluorocarbons:

(1) Metered-dose steroid human drugs for nasal inhalation,

(2) Metered-dose steroid human drugs for oral inhalation,

(3) Metered-dose adrenergic bronchodilator human drugs for oral inhalation,

(4) Contraceptive vaginal foams for human use, and

(5) Metered-dose ergotamine tartrate drug products administered by oral inhalation for use in humans.

(6) Intrarectal hydrocortisone acetate for human use.

(7) Polymyxin B sulfate-bacitracin zinc-neomycin sulfate soluble antibiotic powder without excipients, for topical use on humans.

(8) Anesthetic drugs for topical use on accessible mucous membranes of humans where a cannula is used for application.

(9) Metered-dose nitroglycerin human drugs administered to the oral cavity.

(10) Metered-dose cromolyn sodium human drugs administered by oral inhalation.

(11) Metered-dose ipratropium bromide for oral inhalation.

(12) Metered-dose atropine sulfate aerosol human drugs administered by oral inhalation.

(13) Metered-dose nedocromil sodium human drugs administered by oral inhalation.

(14) Metered-dosed ipratropium bromide and albuterol sulfate, in combination, administered by oral inhalation for human use.

(15) Sterile aerosol talc administered intrapleurally by thoracoscopy for human use.

(f) Any person may file a petition in accordance with part 10 of this chapter to amend paragraph (e) of this section to specify a use of chlorofluorocarbons in a product as not being subject to the adulteration and misbranding provisions in paragraph (c) of this section. The petition must be supported by an adequate showing that:

(1) There are no technically feasible alternatives to the use of a chlorofluorocarbon in the product,

(2) The product provides a substantial health benefit, environmental benefit, or other public benefit that would not be obtainable without the use of the chlorofluorocarbon, and

(3) The use does not involve a significant release of chlorofluorocarbons into the atmosphere or that the release is warranted in view of the consequence if the use were not permitted.

(g) Any holder of an approved new drug application or new animal drug application for a drug product containing a chlorofluorocarbon in a self-pressurized container, except those drug products listed in paragraph (e) of this section, shall submit to the Food

and Drug Administration on or before October 1, 1978, either a supplemental application providing for a revised formulation complying with the requirements of § 314.70 or § 514.8 of this chapter or a letter requesting that a new drug application or a new animal drug application for the drug product containing chlorofluorocarbon be withdrawn and that the right to a hearing on the withdrawal of the application is waived.

(h)(1) Each manufacturer of a drug product listed in paragraph (e) of this section that is not covered by an approved new drug application shall submit a new drug application in accord with § 314.50 of this chapter on or before June 15, 1978.

(2) An abbreviated new drug application conforming to § 314.94 of this chapter is acceptable in lieu of a full new drug application for any product included in the classes of products in paragraph (e) of this section if the product is one that is described under § 314.92 of this chapter. A finding has been made that an abbreviated new drug application may be submitted for the following products included in the classes of products listed in paragraph (e) of this section:

(i) Ergotamine tartrate supplied in a metered-dose aerosol form suitable for oral inhalation for the treatment of migraine headaches. Each measured dose must deliver a dose of the active ingredient equivalent to that contained in the product that has been the subject of a separate finding that an abbreviated new drug application is suitable.

(ii) Isoproterenol hydrochloride supplied in a metered-dose aerosol form suitable for oral inhalation for use as an adrenergic bronchodilator. Each measured dose must deliver a dose of the active ingredient equivalent to that contained in the products that have been the subject of a separate finding that an abbreviated new drug application is suitable.

(iii) Epinephrine, epinephrine bitartrate, or epinephrine hydrochloride (racemic) in a metered-dose aerosol form suitable for oral inhalation for use as an adrenergic bronchodilator. Each measured dose must deliver a dose of the active ingredient

equivalent to that specified in an OTC proposed or final monograph issued under the provisions of 21 CFR part 330.

(iv) Nonoxynol 9 in an aerosol foam suitable for vaginal administration as a contraceptive foam. The aerosol foam must contain 8 to 12.5 percent of nonoxynol 9.

(i) Any sponsor of an "Investigational New Drug Application" (IND) or "Notice of Claimed Exemption for a New Animal Drug" (INAD) for a drug product containing a chlorofluorocarbon shall:

(1) Amend the IND or INAD on or before December 15, 1978, to revise the formulation removing the chlorofluorocarbon.

(2) Submit the information required under paragraph (f) of this section to amend paragraph (e) of this section to show that the use of chlorofluorocarbon is essential, or

(3) Submit the information required under paragraph (j) of this section requesting that studies with the drug product containing a chlorofluorocarbon propellant be allowed to be performed.

(j) Any sponsor of an IND or INAD who wishes to initiate or continue a study beyond December 15, 1978 on a drug product containing a chlorofluorocarbon shall submit a petition in accordance with part 10 of this chapter requesting that studies be permitted to collect the data to show that the use of the chlorofluorocarbon is an essential use. The petitions must be supported by the following:

(1) A description of the drug product,

(2) An explanation why a chlorofluorocarbon propellant is used in the product rather than another propellant or another dosage form of the product, and

(3) The benefit that the investigational product is believed to have and that the sponsor hopes to demonstrate by the studies.

(k) The Commissioner will initiate action to withdraw approval of an application or terminate an IND or INAD notice in accordance with the applicable provisions of section 505 of the act and parts 312 and 314 of this chapter, or section 512 of the act and parts 511 and 514 of this chapter upon failure of a

holder of an approved new drug application or approved new animal drug application or sponsor of an IND or INAD notice to comply with the applicable provisions of this section.

(1) Food, drug, device, or cosmetic products manufactured or packaged on or after December 15, 1978, and finished products initially introduced into interstate commerce on or after April 15, 1979, shall comply with this regulation.

[43 FR 11316, Mar. 17, 1978, as amended at 44 FR 3961, Jan. 19, 1979; 44 FR 30334, May 26, 1979; 45 FR 22902, April 4, 1980; 51 FR 4591, Feb. 6, 1986; 52 FR 15717, Apr. 30, 1987; 54 FR 9034, Mar. 3, 1989; 55 FR 39267, Sept. 26, 1990; 57 FR 17980, Apr. 28, 1992; 58 FR 6088, Jan. 26, 1993; 61 FR 15700, Apr. 9, 1996; 61 FR 25392, May 21, 1996]

PART 3—PRODUCT JURISDICTION

Subpart A—Assignment of Agency Component for Review of Premarket Applications

Sec.

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- 3.2 Definitions.
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- 3.4 Designated agency component.
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Subpart B [Reserved]

AUTHORITY: 21 U.S.C. 321, 351, 352, 353, 355, 360, 360c–360f, 360h–360j, 360gg–360ss, 371(a), 379e, 381, 394; 42 U.S.C. 216, 262.

SOURCE: 56 FR 58756, Nov. 21, 1991, unless otherwise noted.

Subpart A—Assignment of Agency Component for Review of Premarket Applications

§ 3.1 Purpose.

This regulation relates to agency management and organization and has two purposes. The first is to implement section 503(g) of the act, as added by section 16 of the Safe Medical Devices Act of 1990 (Pub. L. 101–629), by specifying how FDA will determine the organizational component within FDA

designated to have primary jurisdiction for the premarket review and regulation of products that are comprised of any combination of a drug and a device; a device and a biological; a biological and a drug; or a drug, a device and a biological. This determination will eliminate, in most cases, the need to receive approvals from more than one FDA component for such combination products. The second purpose of this regulation is to enhance the efficiency of agency management and operations by providing procedures for determining which agency component will have primary jurisdiction for any drug, device, or biological product where such jurisdiction is unclear or in dispute. Nothing in this section prevents FDA from using any agency resources it deems necessary to ensure adequate review of the safety and effectiveness of any product, or the substantial equivalence of any device to a predicate device.

§ 3.2 Definitions.

For the purpose of this part:

(a) *Act* means the Federal Food, Drug, and Cosmetic Act.

(b) *Agency component* means the Center for Biologics Evaluation and Research, the Center for Devices and Radiological Health, or the Center for Drug Evaluation and Research.

(c) *Applicant* means any person who submits or plans to submit an application to the Food and Drug Administration for premarket review. For purposes of this section, the terms “sponsor” and “applicant” have the same meaning.

(d) *Biological product* has the meaning given the term in section 351(a) of the Public Health Service Act (42 U.S.C. 262(a)).

(e) *Combination product* includes:

(1) A product comprised of two or more regulated components, i.e., drug/device, biologic/device, drug/biologic, or drug/device/biologic, that are physically, chemically, or otherwise combined or mixed and produced as a single entity;

(2) Two or more separate products packaged together in a single package or as a unit and comprised of drug and device products, device and biological